

✓
Please amend the specification in adherence with 37 C.F.R. § 1.821-1.825 as follows:

IN THE SPECIFICATION:

Please replace the paragraph beginning on page 5, line 12, with the following amended paragraph:

Fig. 3 Comparison of the heavy chain variable region amino acid sequence of humanized immunoglobulin HuZAF(SEQ ID NO:10) and humanized immunoglobulins haf25(SEQ ID NO:11), and HuXAF(SEQ ID NO:9).

✓
Please replace the paragraph beginning on page 11, line 3, with the following amended paragraph:

Position H11 does not fulfill the criteria for substitution given above, but nevertheless makes a significant contribution to neutralizing activity in humanized immunoglobulins incorporating this substitution. The desirability of substituting at this position was determined by substitution of various positions in a chimeric AF2 antibody (i.e., having mouse variable domains and human constant regions) with amino acids from equivalent positions in the human EU antibody(SEQ ID NOS:12 and 13). Substitution of position H11 caused a significant reduction in the neutralizing activity of the chimeric antibody for γ -IFN.

✓
Please insert the accompanying paper copy of the sequence listing, page numbers 1-9, at the end of the application.

REMARKS

Applicants request entry of this amendment in adherence with 37 C.F.R. §§ 1.821-1.825. The information contained in the computer readable disk of Application No. 09/450,520 was prepared through use of the software program "PatentIn" and is identical to that of the paper copy. This amendment contains no new matter.

Attached hereto is a marked-up version of the changes made to the specification by the amendment. The attached page is captioned "VERSION WITH MARKINGS TO SHOW CHANGES MADE."

PATENT

Respectfully submitted,

J. Wellersdunck

TOWNSEND and TOWNSEND and CREW LLP
Two Embarcadero Center, 8th Floor
San Francisco, California 94111-3834
Tel: (650) 326-2400
Fax: (650) 326-2422
JOL:adm
PA 3183346 v1

[illegible]

[illegible]

Fig. 3 Comparison of the heavy chain variable region amino acid sequence of [mouse AF2,] humanized immunoglobulin HuZAF(SEQ ID NO:10) and humanized immunoglobulins haf25(SEQ ID NO:11), and HuXAF(SEQ ID NO:9).

Position H11 does not fulfill the criteria for substitution given above, but nevertheless makes a significant contribution to neutralizing activity in humanized immunoglobulins incorporating this substitution. The desirability of substituting at this position was determined by substitution of various positions in a chimeric AF2 antibody (i.e., having mouse variable domains and human constant regions) with amino acids from equivalent positions in the human EU antibody (SEQ ID NOS:12 and 13). Substitution of position H11 caused a significant reduction in the neutralizing activity of the chimeric antibody for γ -IFN.